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A PROSPECTIVE STUDY ON PATTERNS OF RENAL DISEASES AND ASSESSMENT OF DRUG RELATED PROBLEMS IN PEDIATRICS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: The pattern of kidney diseases varies from place to place due to genetic differences, access to health care, socioeconomic status, and the pattern of background infections. Drug related problems (DRP's) are frequent in hospitalization were multiple changes in patient's medication regimens and lack of community of care may be accompanied. Objectives: To study the pattern of renal diseases and drug utilization in paediatrics. To evaluate the clinical features and categorise renal diseases based on diagnosis, to identify and assess Drug related problems (DRP's) Methods: A prospective observational study was conducted in a tertiary care hospital among 131 paediatric patients with renal diseases who were admitted to the paediatric wards of our hospital over a period of 6 months. Relevant information was retrieved from direct patient interview and from patient case profiles and classified based on aetiology as Infectious and non-infectious diseases. Results: In a total of 131 patients, renal diseases were most commonly observed in males 70 (55%). Majority patients were in the range of 2-12years age group 89 (60%).Highest number of patients were diagnosed with Nephrotic syndrome 53 (39%) followed by UTI. Mostly prescribed category of drugs was antibiotics 79 (57%). Most observed DRP was untreated indication 114 (57%).Conclusion: It emphasize that the pattern of renal diseases in pediatrics, which are the important cause of morbidity and conclude that the pharmacists assessment of drug related problems and providing interventions is vital for improving optimal pharmacotherapy and quality of life.

Key words: Urinary Tract Infection, Nephrotic syndrome, Drug related problems, Glomerulonephritis.

INTRODUCTION

Patterns of Renal Diseases

The pattern of kidney diseases varies from place to place due to genetic differences, access to health care, socioeconomic status, and the pattern of background infections. These variations could be related to genetic predisposition, environmental factors, or lack of awareness about importance of early diagnosis of such disorders[1]. Children with potentially treatable conditions, e.g. urological, are often referred late with advanced diseases. (CKD) in adulthood[2]. It is known that pattern of kidney diseases may be different in disadvantaged population owing to poverty, poorer access to health care, poorer health seeking behaviors as has been shown for chronic kidney disease[3].

Most Common Prevalent Renal Disorders Include Glomerulonephritis

Glomerulonephritis refers to disorders in which an immunologic insult triggers inflammation and

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proliferation of glomerular tissue with damage to glomerular basement membrane, mesangium of capillary endothelium. Glomerulonephritis may be primary (confined to kidney) or secondary (part of systemic disorder)[4].

Incidence

Acute post-streptococcal GN usually occurs in children older than age of 2 years. The incidence is about 4 times higher in developing countries than in developed countries**.** More common in males than females with peak age onset of 6-7 yrs. It accounts for 90% of renal diseases in childhood per100000 children [5].

Fig: 1 Etiology of Glomerulonephritis in Children [6]

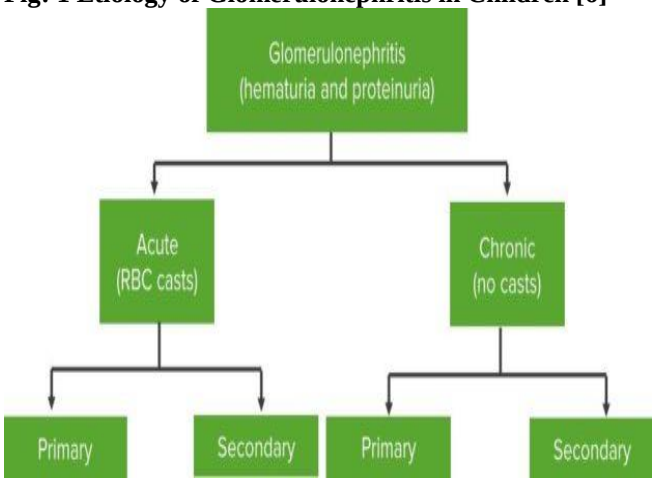
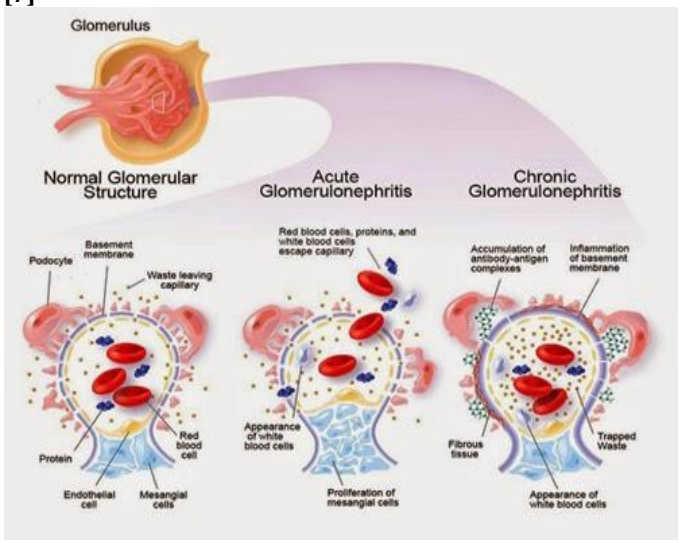


Fig 2: Pathological events in different stages of GMN [7]



Treatment of Glomerulonephritis in Children

The management of GN involves supportive care, as well as treatment of the underlying pathology.

Acute glomerulonephritis

Essentially symptomatic with mild cases of PSGN. Hospital admission is required for those with oligoanuria, moderate to severe edema or hypertension and impaired renal functions. PENCILLIN- For 7 days may be used in those of residual pharyngitis or pyoderma [8]. DIURETICS (FUROSEMIDE):1-3mg/kg helps to manage fluid overload and circulatory congestion. BETA BLOCKERS AND ACE INHIBITORS: Mild hypertension [9]. ORAL/IV FUROSEMIDE and ORAL/SUBLINGUAL NIFEDEPINE: Severe hypertension [10].

Nephrotic syndrome

Nephrotic syndrome is characterized by heavy proteinuria, hypoalbuminemia (albumin<2.5g/dl) and hyperlipidemia [11].

Incidence

Males affected to be more than females to a ratio of 2:1 in children, but this predominance fails to persist in adolescence [12].

Managing nephrotic syndrome:

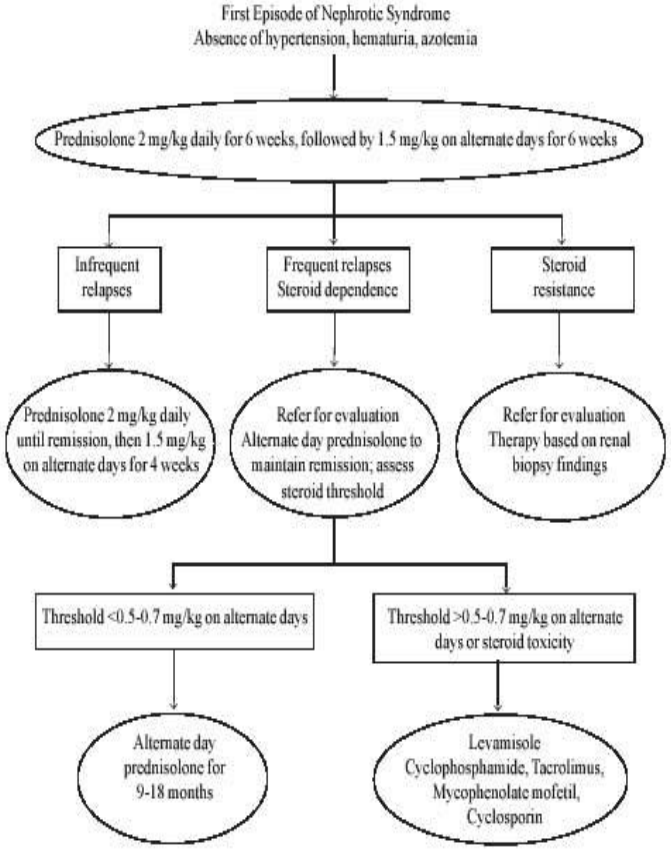


Fig 3: Treatment algorithm for Nephrotic syndrome

Urinary tract infection:

Urinary tract infections (UTI) are common during childhood and often associated with congenital anomalies of the urinary tract and vesicoureteric reflux (VUR), which together consititute an important cause of chronic renal failure. UTI is identified by significant bacteriuria on culture of urine[13].

Incidence

During infancy, the male to female ratio is 3-5:1, Beyond 1 to 2years, there is a female preponderance with male to female ratio of 1:10.

Treatment of UTI in children

Amoxicillin or co-trimoxazole orally are the drugs of choice; oral cephalosporins may be also used. The duration of therapy is 7-10 days. Patients who have high fever, systemic toxicity or flank pain should receive parenteral drugs as described for infants above. Fever should be controlled and a liberal fluid intake provided. The antibiotics may be modified, once the culture and sensitivity results are available. With effective treatment, symptoms disappear within 24-48 hours, urine microscopy does not show bacteria and the culture becomes sterile [14]. Failure to respond suggests bacterial insensitivity to the drugs, lack of compliance to treatment or presence of complicating factors such as obstructive uropathy.

AIM

The main aim of the study is to determine patterns of kidney diseases and to assess the drug related problems among pediatrics in a tertiary care hospital.

OBJECTIVES

1. To study the patterns of renal diseases in pediatrics.
2. To assess the clinical features of renal diseases in pediatrics.
3. To categorize the renal diseases based on diagnosis into Infectious and non-infectious.
4. To study the drug utilization pattern among renal disease paediatric patients
5. To identify and assess drug related problems.

MATERIALS AND METHODS

Study design: Prospective study conducted in Renal Pediatric.

Study site: Department of Pediatrics, Sri Venkateswara Ramnaryan Ruia Government General Hospital, Tirupati

Study duration: 6 months (June 2019-November 2019)

Study population: 131 Population

Study material:

- Patient data collection Proforma
- Informed consent form (ICF)

Tool of casuality Assessment : Naranjo Scale

STUDY CRITERIA:

Inclusion criteria:

- Renal disease patients of either gender who are below 16 years of age in Paediatrics in-patient ward with or without co-morbidities.
- Patients willing to participate in the study.

Exclusion criteria

- Patients unwilling to participate in the study.
- Patients who are mentally retarded.
- Patients who are physically ill.
- Patients with incomplete records were excluded from the study.

Method of Data collection

This prospective study was carried out after obtaining the permission of institutional review board, Sri Padmavathi School Of Pharmacy, Tiruchanoor, Tirupati, A.P, India. All paediatric (<16years) patients with renal diseases admitted in the Pediatrics in-patient ward of Sri Venkateswara Ramnarian Ruya Government General Hospital, between June 2019 to November 2019 were included in the study. Patients with incomplete records were excluded from the study.

Firstly, the data was collected via a specially designed Proforma which includes patient demographics, past medical history, antenatal history, natal history, birth history immunization history, developmental history, family and surgical history, co-morbidities, diagnosis, relevant investigations and present medications prescribed for each patient. The data was obtained by direct patient interview and from patient case profiles and classified based on physician Diagnosis as Infectious and non infectious diseases.

The severity of identified DRP's was classified as major, moderate or minor. The obtained Drug related problems are provided with necessary interventions using Evidence based medicine, Micromedex, CIMS.

Major DRPs were defined as those requiring intervention, otherwise it leads to major or irreversible detrimental effects. Moderate DRPs included DRPs whereby interventions would result in moderate benefit for the patient, while minor DRPs were defined as those requiring only minor adjustments, such as modifications to dosage timings.

The data obtained and the patient related parameters were computed using Microsoft Office and Microsoft Excel 2016. The results were expressed as number and percentage in the form of bar diagram and pie chart or in tabular form.

RESULTS

Out of 131 patients, highest number of patients were with Nephrotic Syndrome 52, and least were renal tubular acidosis in 1 patients respectively (Fig. 4). Among 126 infectious diseases, the highest causative agent were streptococcus (2.8%), candidiasis (2.8%), and least were E. coli, and bacilli (0.7%) (Fig. 5). Out of 131 patients oedema (31%) was observed in higher number of patients and least was seizures (0.4%) (Fig. 6). The highest investigating parameter observed was pus cells (54%) and the least was bacteria (4.6%) (Fig. 8). It was observed that more number of prescriptions are prescribed with 1 antibiotic in 79 (57%) prescriptions, and least was with 4 antibiotic in 4 (2%) prescriptions (Fig. 9).

From obtained data, the most encountered Drug related problem were untreated indication 41%, and the

least were drug use without indication 1% (Fig. 9). Out of 46 drug interactions, 88% with moderate drug interactions and 9% with major drug interactions and 3% with minor drug interactions (Fig. 10). From the above data, we can understand that more number of recommendations were provided to prescriber (51%) and least were to nurse (10%) (Fig. 11). Among 131 prescriptions ceftriaxone induced loose stools were shown mostly i.e. 4 (40%) prescriptions, and least was pantoprazole induced constipation in 1(10%) prescriptions (Fig. 12).

Fig: 4 Etiological classification of renal diseases in children

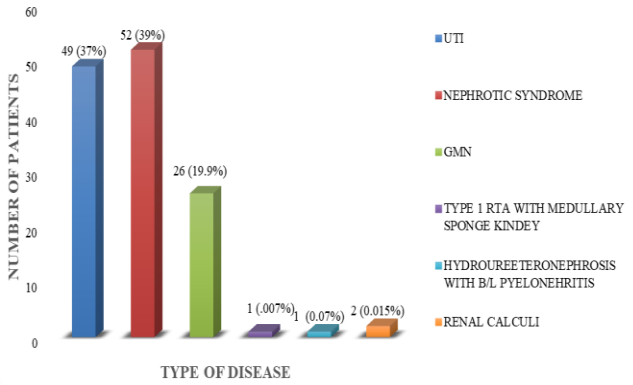


Fig 5: Causative agents of infectious renal diseases in pediatrics

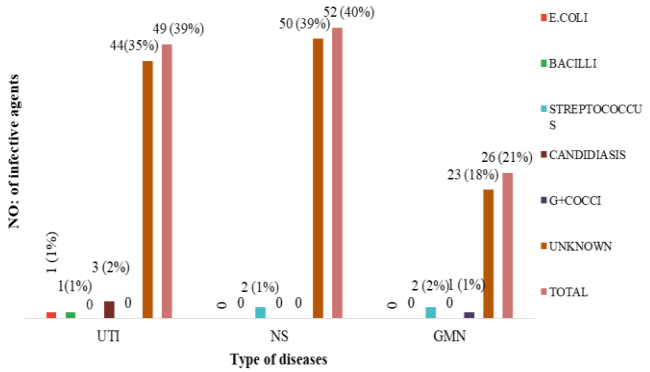


Fig: 6. Clinical features distribution among various renal disorders

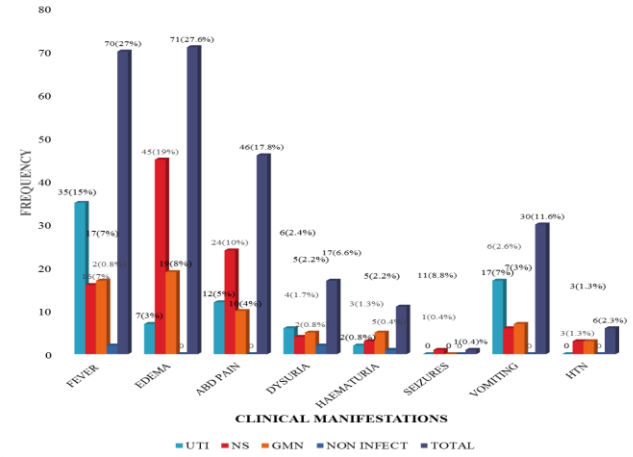


Fig: 7. Investigational profile of renal diseases

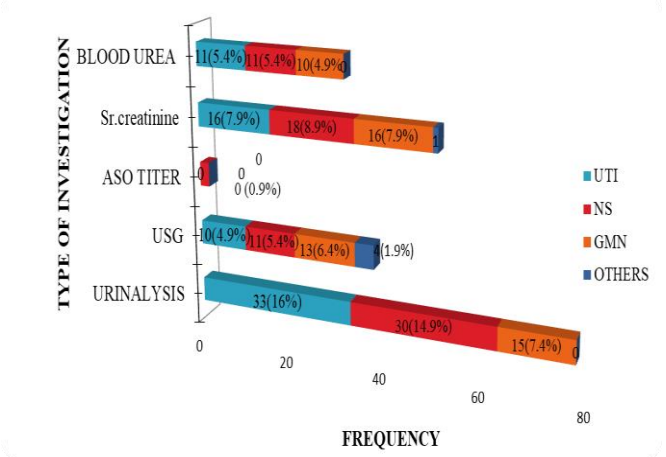


Fig: 8. Analysis of urinary parameters in infectious renal disorders

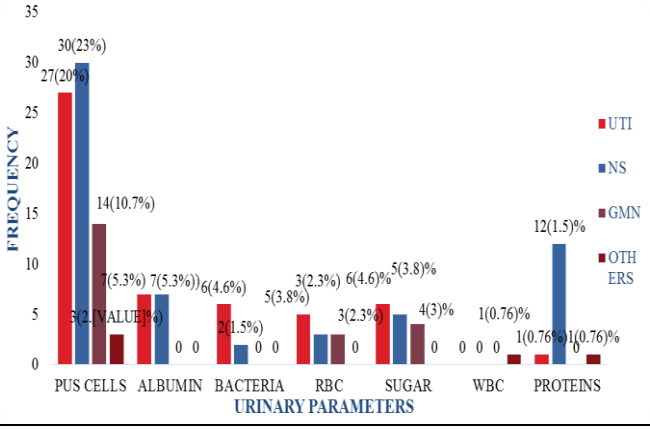


Fig: 9. No. of antibiotics per prescription in infectious renal diseases

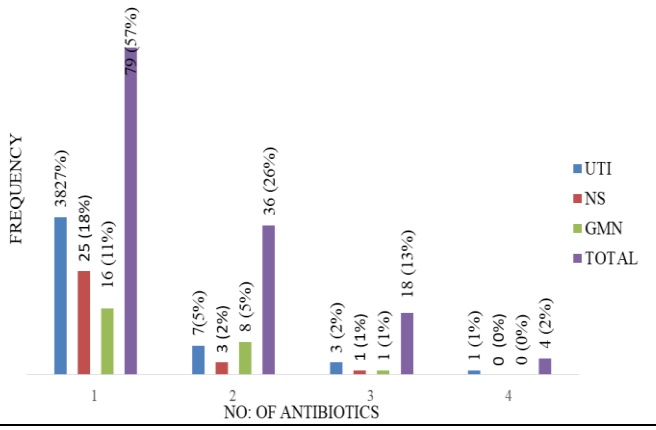


Fig: 10. Drug related problems classification

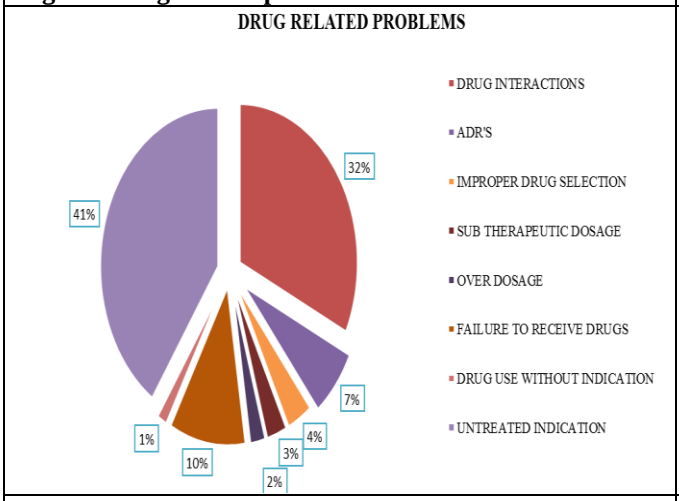


Fig: 11. Drug interactions classification

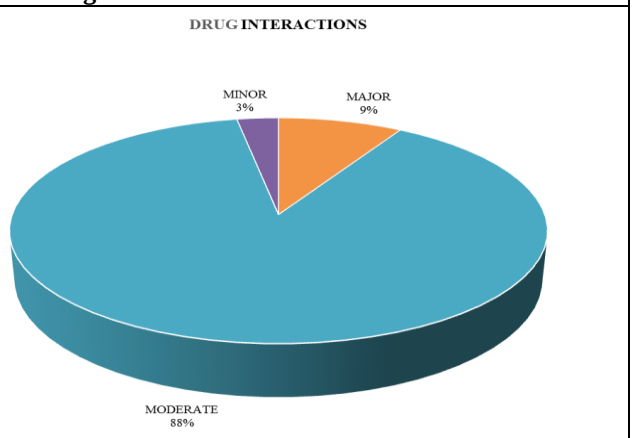


Fig: 12. Interventions for drug related problems

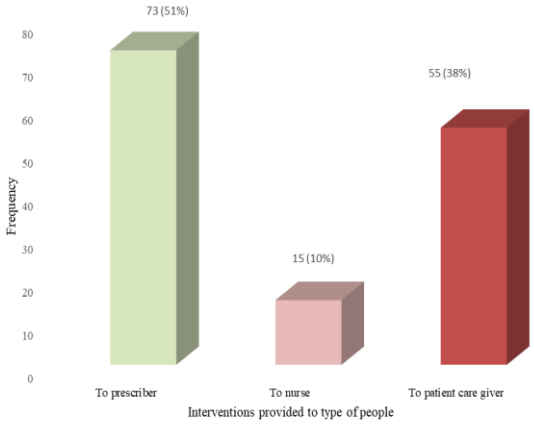


Fig: 13. Drugs involved in adverse effects

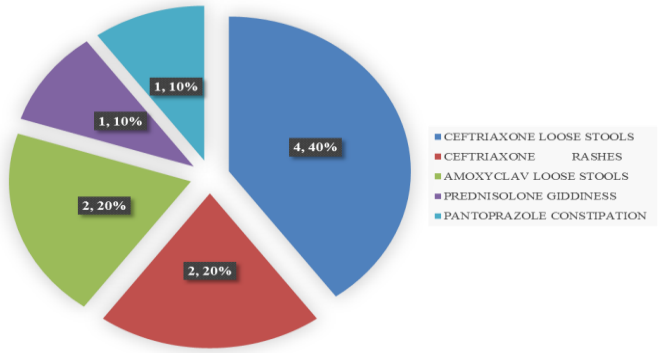


Table 1. Assesment of Drug Related Problems

Type Of Intervention	Results	No of Patients
Untreated indication	Fever	5
n =58	Cold	4
	Facial puffiness	5
	Cough	11
	Edema	6
	Abdominal pain	8
	Loose stools	3
	Vomitings	10
	Rashes	1
	Abdominal distention	5
Drug use without indication	Ondansetron –patient do not have vomitings	2
n= 24	Paracetamol –no fever	4
	Syp Chlorpheneramine maleate - no cold/itching	2
	Nifedipine – BP is normal	13
	Ranitidine–no gastritis	1
	Enalapril – no HTN	2
Sub therapeutic dosage	Syp Ambroxyl-was given OD instead of TID for severe cough	2

n= 4	Syp Paracetamol-was given OD instead of TID to treat fever	2
Over dosage n= 3	Anti-Hypertensive drugs (Nifidipine,Enalapril,furosimide)	2
	Prednisolone	1
ADR's	Ceftriaxone –induced loose stools	4
n= 10	Ceftriaxone – induced rashes	2
	Amoxicillin+ clavulonic acid – induced loose stools	2
	Prednisolone – induced dizziness	1
	Pantoprazole- induced costipation	1
Failure to receive drug	Ambroxyl –out of stock	4
n= 15	Anti-Hypertensive drugs	2
	B-complex-out of stock	5
	Furosemide	2
	Pantoprazole	2
Improper drug selection	Amikacin-The patient is resistant to Amikacin, but they prescribed it.	2
n=5	Cough-cannot treated by cetrizine.	3

Table 2. Recommendations for Drug Related Problems

DRP	Action Recommended	Total	Percentage
Untreated indication-58	Add drug by discussion with prescriber	73	51
Adverse drug reactions- (10)	Change drug by discussion with prescriber		
	Dose reduction by discussion with prescriber		
Improper drug selection- 5	Change drug by discussion with prescriber		
Drug interactions Major-6	Duration change by discussion with nurse	15	10
Sub therapeutic dose-4	Changed to correct dose by discussion with nurse		
Over dose-3	Dose decreased by discussion with nurse		
Drug use without indication-2	Remove the unwanted drugs by discussing with nurse		
Drug interactions-minor and moderate(40)	Changed duration by discussion with prescriber	55	38
Failure to receive drugs(15)	Advised to take drugs properly.		
Drug interactions-minor and moderate(40)	Drug interactions-minor and moderate(40)		

Table 3. Drug Interactions in Study Population

S.No	Drugs Involved	Severity	Outcome	Mangement	No. of Cases	Percentage (%)
1	Nifedipine and prednisolone	Moderate	Prednisolone decreases the effect of Nifedipine	Blood pressure should be monitored on prolonged corticosteroid therapy	13	28
2	Prednisolone and Meropenem	Moderate	Prednisolone decrease the effect of Meropenem	Frequent monitoring	2	4.3
3	Nifedipine and Dexamethasone	Moderate	Dexamethasone may reduce the effects of Nifedipine	Dose adjustment	1	2.15
4	Prednisolone and Enalapril	Moderate	Prednisolone reduces the effect of Enalapril.	Dose adjustment	3	6.5
5	Furosemide and Cefixime	Moderate	This combination may cause kidney problems.	Dose adjustment	1	2.17

6	Furosemide and Pantoprazole	Moderate	Hypomagnesaemia, palpitations, seizures	Frequent monitoring	1	2.17
7	Furosemide and Prednisolone	Moderate	This combination may cause muscle pain, loss of appetite, dizziness	Dose adjustment	5	10.8
8	Cefotaxime and Amikacin	Moderate	decreases the effect of Amikacin	Dose adjustment	5	10.8
9	Nifedipine and Hydrocortisone	Moderate	Hydrocortisone may reduce the effects of Nifedipine	Dose adjustment	1	2.17
10	Ceftriaxone and Amikacin	Moderate	This combination leads to increased risk of kidney damage	Dose adjustment	4	8.6
11	Piperacillin tazobactam and Amikacin	Moderate	Piperacillin may reduce the effects of amikacin	Dose adjustment	2	4.3
12	Pantoprazole and Amikacin	Moderate	This combination leads to increased risk of hypomagnesaemia which results in arrhythmias, palpitations, muscle spasm and tremors	Dose adjustment	1	2.17
13	Nifedipine and Enalapril	Minor	Nifedipine decreases the effectiveness of enalapril in lowering blood pressure	Dose adjustment	1	2.17
14	Amikacin and Furosemide	Major	This combination leads to increased risk of hearing loss, ringing in the ears and kidney damage	Dose adjustment	1	2.17
15	Isoniazid and Paracetamol	Major	Cause serious side effects that effects liver	Dose adjustment	2	4.3
16	Rifampicin and Nifedipine	Major	Rifampin significantly reduce the blood levels of Nifedipine	Dose adjustment	2	4.3
17	Doxycycline and Piperacillintazo bactam	Major	Concurrent use of these drugs leads to decreased antibacterial effectiveness	Avoid concurrent use	1	2.17
				TOTAL	46	

Table 4. Adverse Reactions Observed in Study Population

S.No	Drug Involved	Adverse Event Observed (n=10)	Casuality Assesment (Naranjo scale)	Treatment	No. Of prescriptions	Percentage (%)
1	Ceftriaxone	Loose stools	Probable (7)	Specific	4	40
2	Ceftriaxone	Rashes	Probable (7)	Symptomatic	2	20
3	Amoxicillin + Clavulonic acid	Loose stools	Probabale (6)	Specific	2	20
4	Prednisolone	Giddiness	Possible (4)	Symptomatic	1	10
5	Pantoprazole	Constipation	Possible (4)	Symptomatic	1	10
				Total	10	100%

DISCUSSION

Renal disease is a major cause of morbidity and mortality. Paediatric patients with renal disease especially younger ones may present with nonspecific signs and symptoms unrelated to urinary tract. The pattern of paediatric kidney diseases varies according to genetic, racial, environmental differences as well as geographical locations.

Drug utilization has been identified as the marketing, distribution, prescription and use of drugs on society with special emphasis on the resulting medical and social consequences. Drug utilization studies are playing a major role in identifying any faults in the therapy and also find out solutions to rectify the same.

The special care in their medication should be very much needed in order to avoid drug related problems. Our study reveals the need of pharmacist to make recommendations for rationalised drug therapy among paediatrics populations.

The present study was conducted in a government general hospital.Total 131 patients were included in the study. Among them70 (53%) were males and 61(47%) were females. This is not surprising as the renal diseases are known to be commoner in males because of the higher frequency of Congenital Anomalies of Kidney and Urinary Tract (CAKUT) in males.

The study revealed that majority of the patients were found to be in between the age group 2-15 years were 102 (77.86%) patients, followed by 1- 2years were 28 (36%) because in infants and children birth defects, congenital abnormalities, and hereditary diseases are the most common causes of kidney damage.

In this study, the infectious disorders were Nephrotic syndrome 52(39%) was our leading diagnosis, followed by Urinary tract infection 49(37%), Glomerulonephritis 26(19.9%) patients. The reasons for this are not clear and may reflect the interplay of various factors in the etiopathogenesis of Nephrotic Syndrome. But the differences across different regions could be accounted for by the differences in environmental factors, such as poor hygiene, poverty, and socioeconomic conditions, as well as genetic factors and late presentation may have influenced the rates of childhood kidney diseases.

The non-infectious renal disorders encountered were Renal stones 2(1.5%) patients, followed by Hydroureteronephrosis with bilateral pyelonephritis 1(0.75%) patients, Type 1 RTA with medullary sponge kidney 1(0.75%) patients. The high incidence of renal calculi in our study may related to hot weather as well as nutritional or genetic factors.

In the total study population, the most common clinical manifestations observed were edema in 71(27.6%) patients, followed by fever 70 (27%) patients, abdominal pain 46 (17.8%) patients, dysuria 17 (6.6), Haematuria 11 (4.2%) patients, Hypertension 6 (2.3%) patients, seizures 6 (2.3%) patients, vomiting 30 (11.6%) patients because initial clinical presentation may vary from centre to centre and it mainly depends on the stage of disease and underlying aetiologies.

Among infectious renal diseases in this study, the most causative organisms are Staphylococcus aureus in 4 (4.4%) patients, followed by Candida species in 3 (3.3%) patients and E. coli in 2 (2.2%) patients.

Drug utilisation studies have the potential to make objective evaluation and analysis of health professional's work. In Renal diseases, majority of patients were prescribed with antibiotics 137(28.96%).The most prescribed antibiotic is ceftriaxone 52(38%).

In overall study population, the highest number of drugs per prescription are 3 (32%) and the majority of prescriptions are with 1 (57%) antibiotic. In total study population, 85 drug related problems were found. The majority in DRP's are untreated indication 114 (57%) patients, followed by drug-drug interactions 46 (26%), failure to receive drugs 15 (8%), adverse drug reactions 10 (5%), improper drug selection 5 (3%), sub-therapeutic dose 4 (2%), and over dose 3 (2%) and Drug use without indication 2 (1%).

Various factors like gender, age, duration of hospital stay, inter current diseases and polypharmacy are the contributing factors for the occurrence of drug related problems. The most frequent DRP in our study is untreated indication for facial puffiness and edema which is most encountered renal manifestation. This is may be due to peak hour and lack of time to the physicians.

Then, the drug interaction was the predominantly occurring problem. In this study mostly DI's (26%) occurs between the corticosteroids and antihypertensive which are major class of drugs in treating renal disorders. This may be because of lack of physician knowledge about drugs and poly-pharmacy.

Another DRP found is failure to receive drugs(8%) which occurs at patient level due to factors like halting the medicines as soon as symptoms subsides, poverty and less knowledge regarding the medicines.

ADR (5%) is mostly associated with the use of antibiotics in this study. The main reason for this are due to lack of hypersensitivity testing and therapeutic drug monitoring. Another DRP found was improper drug selection (3%) and the contributing factor was mainly improper prescribing by physician, improper nursing and pharmacist supervision.

Remaining DRP's such as sub therapeutic dose and over doses were encountered at 2% and 1% respectively in this study. Generally inappropriate doses are common in paediatrics than adults because of weight based dosing calculations, fractional dosing.

Thus many factors are associated with DRP's in children, the associations are cumulative and interdependent. So there is need of clinical pharmacists to assist in preventive strategies and extends the support by

providing interventions in order to optimise the pharmacotherapy.

CONCLUSION

Our study emphasize that the patterns of renal diseases in pediatrics, which are important cause of morbidity. We all know that drugs can be useful tools in the prevention and treatment of symptoms and diseases, but if not used properly, they may be harmful and cause new symptoms or produce sub-optimal effects which are termed as DRP's. The role of a clinical pharmacist in this situation appears to be a strong intervention and very crucial one which depends on the pharmaceutical services by bringing those problems to the notice of physician and other health care professionals and take precautions and measures to avoid them. The present study points to the establishment of a DRP's reporting system at each hospital and to share the data with other hospitals/health care settings. The study conclude that the pharmacists and general practitioners can work together to identify and resolve DRP's in order to improve safety and quality of life of patients.

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